

AMENDMENTS TO THE SPECIFICATION

Please enter the attached Sequence Listing. The sequence listing does not constitute new matter.

Please amend the specification as follows. Insertions and deletions are indicated by underlining and strikethrough text, respectively.

Please amend the paragraph beginning on page 57, line 23 as follows:

In a first PCR, the repertoire of both conventional (1.6 kb) and heavy-chain (1.3 kb) antibody gene segments were amplified using a leader specific primer (5'-GGCTGAGCTCGGTGGTCCTGGCT-3'; SEQ ID NO:85) and the oligo d(T) primer (5'-AACTGGAAGAATTCGCGGCCGCAGGAATTTTTTTTTTTTTTTTTTTT-3'; SEQ ID NO:86). The resulting DNA fragments were separated by agarose gel electrophoresis and the 1.3 kb fragment encoding heavy-chain antibody segments was purified from the agarose gel. A second PCR was performed using a mixture of FR1 reverse primers (WO03/054016 sequences ABL037 to ABL043) and the same oligo d(T) forward primer.

Please amend the paragraph beginning on page 64, line 22 as follows:

In a first PCR, the repertoire of both conventional (1.6 kb) and heavy-chain (1.3 kb) antibody gene segments were amplified using a leader specific primer (5'-GGCTGAGCTCGGTGGTCCTGGCT-3'; SEQ ID NO:87) and the oligo d(T) primer (5'-AACTGGAAGAATTCGCGGCCGCAGGAATTTTTTTTTTTTTTTTTTTT-3'; SEQ ID NO:88). The resulting DNA fragments were separated by agarose gel electrophoresis and the 1.3 kb fragment encoding heavy-chain antibody segments was purified from the agarose gel. A second PCR was performed using a mixture of FR1 reverse primers (WO03/054016 sequences ABL037 to ABL043) and the same oligo d(T) forward primer.

Please amend the paragraph beginning on page 71, line 1 as follows:

In a first PCR, the repertoire of both conventional (1.6 kb) and heavy-chain (1.3 kb) antibody gene segments were amplified using a leader specific primer (5'-GGCTGAGCTCGGTGGTCCTGGCT-3'; SEQ ID NO:89) and the oligo d(T) primer (5'-

AACTGGAAGAAATTCGCGGCCGCAGGAATTTTTTTTTTTTTTTT-3'; SEQ ID NO:90).

The resulting DNA fragments were separated by agarose gel electrophoresis and the 1.3 kb fragment encoding heavy-chain antibody segments was purified from the agarose gel. A second PCR was performed using a mixture of FR1 reverse primers (WO03/054016 sequences ABL037 to ABL043) and the same oligo d(T) forward primer.

Please amend the paragraph beginning on page 75, line 18 as follows:

The CDR3 region of VHH#3E was amplified by using a sense primer located in the framework 4 region (Forward: CCCCTGCCCCAGTAGTTATACG; SEQ ID NO:91) and an anti-sense primer located in the framework 3 region (Reverse: TGTGCAGCAAGAGACGG; SEQ ID NO:92).

In order to clone the CDR-3 fragment in pAX10, a second round PCR amplification was performed with following primers introducing the required restriction sites:

Reverse primer Sfi1:

GTCTCGCAACTGCGGCCAGCCGGCCTGTGCAGCAAGAGACGG (SEQ ID NO:93)

Forward primer Not1:

GTCTCGCAACTGCGGCCGCCCTGGCCCCAGTAGTTATACG (SEQ ID NO:94)

Please amend the paragraph beginning on page 83, line 14 as follows:

Peripheral blood lymphocytes (PBLs) are isolated by centrifugation on a density gradient (Ficoll-Paque Plus Amersham Biosciences). PBLs and lymph node are used to extract total RNA (Chomczynski and Sacchi 1987) followed by synthesis of cDNA using a hexanucleotide random primer. The repertoire is amplified using two hinge-specific primers:

AACAGTTAAGCTTCCGCTTGCGGCCGCGGAGCTGGGGTCTTCGCTGTGGTGCG (SEQ ID NO:95) and
AACAGTTAAGCTTCCGCTTGCGGCCGCTGGTTGTGGTTTGGTGTCTTGGGTT (SEQ ID NO:125) and a framework 1 specific primer: GAGGTBCARCTGCAGGASTCYGG (SEQ ID NO:96).

Please amend the paragraph beginning on page 86, line 16 as follows:

A functional portion, the CDR3 region of MP2F6SR, was amplified by using a sense primer located in the framework 4 region (F6 CRD3 Forward:CTGCCCCAGAAGTCATACC; SEQ ID NO:97) and an anti-sense primer located in the framework 3 region (F6 CDR3 Reverse primer:TGTGCATGTGCAGCAAACC; SEQ ID NO:98).

In order to fuse the CDR-3 fragment with the anti-serum albumin VHH MSA-21, a second round PCR amplification was performed with following primers:

F6 CDR3 Reverse primer Sfi1:

GTCTCGCAACTGCGGCCAGCCGGCCTGTGCATGTGCAGCAAACC (SEQ ID NO:99)

F6 CDR3 Forward primer NotI:

GTCTCGCAACTGCGGCCGCGCTGGCCCCAGAAGTCATACC (SEQ ID NO:100)

Please replace the Table beginning on page 92, which is referred to as “Table 13: Primer sequences”, with the following amended Table:

Name	<u>SEQ ID NO</u>	Sequence 5' – 3'
ABL002	<u>101</u>	GGCTGAGCTCGGTGGTCCTGGCT
ABL010	<u>102</u>	AACTGGAAGAATTCGCGGCCGAGGAATTTTTTTTTTTTTTTT
ABL037	<u>103</u>	CATGCCATGACTCGCGGCCAGCCGGCCATGGCCGAGGTGCAGCTGGT GGAGTCTGG
ABL038	<u>104</u>	CATGCCATGACTCGCGGCCAGCCGGCCATGGCCGATGTGCAGCTGGT GGAGTCTGG
ABL039	<u>105</u>	CATGCCATGACTCGCGGCCAGCCGGCCATGGCCGCGGTGCAGCTGGT GGAGTCTGG
ABL040	<u>106</u>	CATGCCATGACTCGCGGCCAGCCGGCCATGGCCGCCGTGCAGCTGGT GGATTCTGG
ABL041	<u>107</u>	CATGCCATGACTCGCGGCCAGCCGGCCATGGCCCAGGTGCAGCTGGT GGAGTCTGG
ABL042	<u>108</u>	CATGCCATGACTCGCGGCCAGCCGGCCATGGCCCAGGTACAGCTGGT GGAGTCTGG
ABL043	<u>109</u>	CATGCCATGACTCGCGGCCAGCCGGCCATGGCCCAGGTAAAGCTGGA GGAGTCTGG
geneIII	<u>110</u>	CCACAGACAGCCCTCATAG
M13 rev	<u>111</u>	GGATAACAATTCACACAGG

Table 13: Primer sequences